

Melatonin level and sleep disorders in adolescents

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Abstract

Background Sleep disorder is defined as a disturbance in the quality and time of sleep. Decreased melatonin levels have been noted in people with sleep disorders. Melatonin is a neurohormone, produced mainly by the pineal gland, as well as a small part of the retina. Its function is to maintain normal circadian rhythms and it is related to sleep regulation in humans.

Objective To assess for a relationship between melatonin levels and sleep disorders in adolescents.

Methods We conducted a cross-sectional study on students of two secondary schools in Tuminting, Manado, North Sulawesi, from May to June 2013. Subjects were obtained by consecutive sampling for a total of 44 adolescents aged 12-15 years. Subjects filled questionnaires, underwent wrist actigraphy, and provided blood specimens for examination of melatonin levels. We used descriptive and logistic regression analyses to assess for relationships between variables.

Results Thirty (68.2%) subjects experienced sleep disorders. There was a significant association between decreased melatonin levels and the higher incidence of sleep disturbances ($P = 0.02$).

Conclusion There is a correlation between melatonin levels in adolescents with sleep disorders. Decreased melatonin levels are associated with sleep disorders. [Paediatr Indones. 2015;55:215-18].

Keywords: melatonin, sleep disorders, adolescents

Sleep is important for the physical growth and intellectual development of children. Sleep disorders in adolescents are influenced by many factors, both medical and non-medical. Adolescents may experience dramatic changes in their sleep-wake patterns, including reduced sleep duration, delayed sleep time, and different sleep patterns on school days and weekends. Thus, teens' quality of sleep tends to diminish compared to that during childhood. In the last decade, epidemiological studies have revealed that an increased number of adolescents experience sleep disorders. A previous study used the *Sleep Disturbance Scale for Children* (SDSC) and wrist actigraphy found that in children aged 12-15 years, around 62.5% using SDSC and the 65.6% using wrist actigraphy experienced sleep disorders.¹ Likewise, another study used the SDSC for children aged 12-15 years and found that 62.9% had sleep disorders, with wake transition disorders being the most common.²

The sleep-wake state varies in the relative level of motor activity, with reduced activity during sleep.³ The wrist actigraph unit records the cycles of movement during sleep and waking. It is not invasive and uses a multidirectional, piezoelectric accelerometer to record the degree and intensity of motoric movement. The

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wrist actigraph unit is worn like a wrist watch, easy to use, and battery-operated.⁴

The teenage years are considered to have the most potential for sleep disorders compared to other age groups of children and adults. Melatonin levels in teens may be related to their sleep habits. To date, there has been little research on adolescent melatonin levels and sleep disorders.

The aim of this study was to assess for a possible correlation between melatonin levels and sleep disorders in adolescents.

Methods

We conducted a cross-sectional study. The study was performed from May to June 2013 on students of government middle schools SMP Negeri III and SMP Negeri V at Tuminting, Manado, North Sulawesi. The inclusion criteria were teens aged 12 - 15 years who agreed to answer questionnaires, undergo wrist actigraphy, and provide blood specimens for melatonin measurements. We excluded teens in therapy for sleep disorders, those with behavioral disorders such as attention deficit hyperactivity disorder (ADHD), or organic disorders such as hypertension, diabetes mellitus, or anemia. We also excluded teens who consumed drugs and herbs that influenced sleep, did not correctly install their wrist actigraph unit, did not give their address or phone number, or resided outside Manado. This study was approved by the Ethics Committee of Prof. Dr. R.D. Kandou Hospital, Manado. Subjects' parents provided informed consent. We used consecutive sampling to obtain our study population, with each patient who met the study criteria being included in the study until the required sample size was met.

The school principals gave permission for us to recruit subjects from their schools. Consent forms were given to students for their parents approval. We performed history-taking and physical examinations in the school health unit. Interviews and wrist actigraph unit installation was done at subjects' homes. The wrist actigraph unit was worn on the non-dominant arm to reduce the recording of movement in subjects with high mobility. Wrist actigraphy was performed for one night, from 8 pm until the next morning when the subjects awoke. Subjects were asked to record the times they went to sleep and awoke. Wrist

actigraphy indicated the presence of a sleep disorder if one of three parameters were met: sleep efficiency < 85 %, sleep onset latency > 20 minutes, or wake after sleep onset (WASO) > 40 minutes.^{1,4}

Melatonin levels were checked at the next morning between 6:00-7:00 am. Subjects' blood was drawn from a peripheral vein by a laboratory worker who visited their homes. Melatonin level was measured using an ELISA method. Parents were given the examination results. For subjects with serious sleep disorders, we suggested that parents observe their teens' sleep patterns on regular basis, and have them reexamined if necessary.

We used descriptive analysis on the data characteristics and logistic regression analysis to assess for a relationship between melatonin levels and sleep disorders in adolescents. Results were considered to be significant for P value < 0.05. The data were processed with SPSS for Windows version 21 software.

Results

Forty-four adolescents were included in our study. Thirty (68.2%) subjects had sleep disorders. The characteristics of subjects are shown in **Table 1**.

Comparison of melatonin levels between normal adolescent and those with sleep disorders are shown in **Table 2**.

Logistic regression analysis revealed a significant negative correlation between melatonin levels and the incidence of sleep disturbance (P = 0.02) where the lower levels of melatonin, the greater the chance of sleep disorders (**Figure 1**).

Discussion

We aimed to assess for a possible correlation between melatonin levels and sleep disorders in adolescents in 44 junior high school students aged 12-15 years. This age group generally displays changes in sleep cycles and circadian rhythm sleep patterns. Based on wrist actigraphy results, we found 30 (68.2%) adolescents with sleep disorders and 14 (31.8%) adolescents without sleep disorders. Similarly, previous studies estimated that about 62.5% of adolescents aged 12-15 years old have trouble sleeping.^{1,2}

Table 1. Characteristics of study subjects

| Melatonin levels | N = 44 |
|--|---------------|
| Characteristics | |
| Male, n(%) | 27 (61.4) |
| Male with sleep disorders, n | 20 |
| Female, n(%) | 17 (38.6) |
| Female with sleep disorders, n | 0 |
| Mean age (SD), years | 13.41 (1.1) |
| Nutritional status, n (%) | |
| Overweight | 5 (11.4) |
| Normal weight | 33 (75.0) |
| Underweight | 6 (13.6) |
| Mean body weight (SD), kg | 47.34 (16.1) |
| Mean height (SD), cm | 153.05 (14.9) |
| Duration of sleep, n (%) | |
| 3 – 4 hours | 4 (9.1) |
| 5 – 6 hours | 14 (31.8) |
| 7 – 8 hours | 16 (36.4) |
| > 8 hours | 10 (22.7) |
| Extracurricular activity time per week, n (%) | |
| < 4 hours | 30 (68.2) |
| > 5 hours | 14 (31.8) |
| TV and computer time per day, n (%) | |
| 1 hour | 10 (22.7) |
| 2 hours | 23 (52.3) |
| 3 hours | 9 (20.5) |
| 4 hours | 2 (4.5) |
| Played on a cellphone before sleeping, n (%) | |
| Yes | 30 (68.2) |
| No | 14 (31.8) |
| Sleep alone, n (%) | |
| Yes | 38 (86.4) |
| No | 6 (13.6) |
| Wrist actigraphy results , n (%) | |
| Sleep disorders | 30 (68.2) |
| Normal | 14 (31.8) |

girls was not significantly different.¹ Also, Seo *et al.* in Korea found no difference between the incidence of sleep disorders in males and females.¹⁰

We found that duration of sleep needed per day was 7-8 hours in 16 teens and 5-6 hours in 14 teens. However, Seo *et al.* found the average total sleep time required was 8 hours and 41 (SD 51) minutes.¹⁰ In addition, Short *et al.* found that teens reported a mean sleep duration of 6 hours 52 (SD 57) minutes per day, ranging from 3 hours 57 minutes to 9 hours 10 minutes.¹¹

Our subjects had the following TV/computer game habits: 23 subjects (52.3%) spent 2 hours per day, 10 subjects (22.7%) spent 1 hour per day, and 9 subjects (20.5%) spent 3 hours per day. A previous study in 2004 found that approximately 23.5 to 35% of adolescents had a mean TV-watching time of 3 – 3.5 hours per day, and played computers for 30 minutes - 1 hour per day.¹² Times have changed since 2004, with more teens now exposed to more electronic media. In 2010, Shockat *et al.*¹³ reported that approximately 60% of adolescents had a mean TV-watching duration of 2 hours 46 minutes per day, played computer for a mean of 1 hour 17 minutes per day, and had a mean total sleep time of 7 hours 22 minutes per day. Electronic media usage may lead to

Table 2. Distribution of melatonin levels of adolescents with and without sleep disorders

| Melatonin levels | Mean (SD) , pg/mL | 95% CI |
|--------------------------------|-------------------|----------------|
| Without sleep disorders (n=14) | 49.69 (7.70) | 45.24 to 54.13 |
| With sleep disorders (n=30) | 31.37 (6.88) | 28.80 to 33.94 |
| Total (N=44) | 37.20 (11.15) | 33.81 to 40.59 |

Melatonin (*N-acetyl-5-methoxytryptamine*) is an endogenous indoleamine neurohormone that is primarily produced by the pineal gland and a small portion of the retina. Generally produced at the back of the third ventricle in the brain, it acts as a “chronobiotic” to maintain normal circadian rhythm and regulate sleep in humans.^{5,6} Melatonin secretion and circadian rhythm is related to light-dark cycles, light suppress melatonin production, and with the onset of darkness, melatonin is produced and released from pinealocytes.⁷

In our study of 44 adolescents, there were more boys than girls (27 vs. 17, respectively.) We found sleep disorders in 20/27 boys and in 10/17 girls. In contrast, other studies found that females experienced more sleep disorders than males.^{8,9} However, Natalita *et al.* observed that the risk of sleep disturbances in boys and

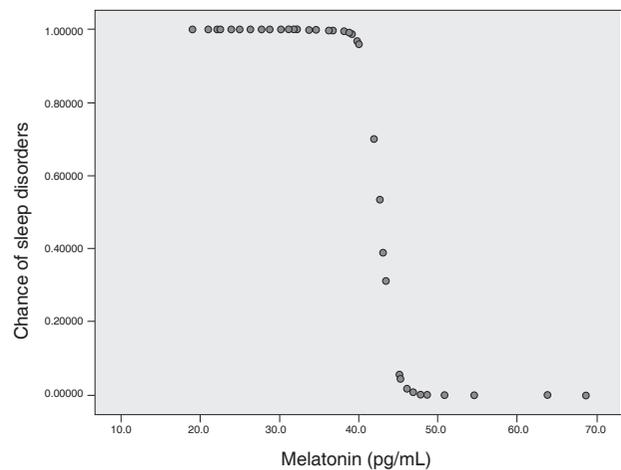


Figure 1. Scatterplot correlation between melatonin levels and sleep disorders

prolonged sleep onset latency and sleep deprivation due to the replacement of sleep time. Two studies found that children who viewed television and computers before bed time had a later bed time and reduced total sleep time.^{11,13}

Thirty subjects (68.2%) used mobile phones before sleeping hours. Van den Bulck *et al.* found that in teens who used cell phones during sleeping hours, 22.1% received messages, 20.6% sent messages, 21.7% received calls, and 14.5% made calls. This mobile phone activity during sleep hours may increase fatigue during the day and interfere with the learning process at school.¹³

In our subjects, 13.6% were not sleeping alone. Co-sleeping is a cause of sleep disorders in children. A previous study revealed subjects gave the following reasons for not sleeping alone: afraid to be alone in the room, wanted to be closer to parents, or not having enough room.¹⁵

Another previous study found a highly significant relationship between salivary and urinary melatonin levels and the incidence of sleep disturbances ($P < 0.01$; $r > 0.7$).¹⁶ In contrast, we used an ELISA method to measure serum melatonin levels. We also found a significant association between melatonin levels and the incidence of sleep disorders ($P = 0.02$). These results suggest that the lower levels of melatonin, the greater the chance of sleep disorders. This study was the first conducted in Manado, North Sulawesi, Indonesia to assess for a relationship between melatonin and sleep disorders in junior high school students. We found that lower melatonin levels were associated with sleep disturbances. Some limitations of this study were its cross-sectional design and the one-time examination of melatonin levels, after a wrist actigraphy. Serial melatonin measurements would allow us to see the exact time of peak increase in melatonin.

In conclusion, decreased melatonin level is associated with sleep disorders in adolescents.

Conflict of interest

None declared.

References

1. Natalita C, Sekartini R, Poesponegoro H. Sleep Disturbance

Scale for Children (SDSC) as a screening instrument sleep disorders in junior high school. *Sari Pediatri*. 2011;12:365-72.

2. Haryono A, Rindiarti A, Arianti A, Pawitri A, Ushuluddin A, Setiawati A, *et al.* Prevalence of sleep disorders in adolescents age 12-15 years in junior high school. *Sari Pediatri*. 2009;11:149-154.

3. Soetjningsih. Pertumbuhan somatik pada remaja. In: Soetjningsih, editor. *Buku ajar tumbuh kembang remaja dan permasalahannya*: 1st ed. Jakarta: CV Sagung Seto; 2004. p. 1-22.

4. Morgenthaler T, Alessi C, Friedman L, Owens J, Kapur V, Boehlecke B, *et al.* Practice parameters for the use of actigraphy in the assessment of sleep and sleep disorders: an update for 2007. *Sleep*. 2007;30:519-29.

5. Elliott P. Melatonin deficiency. Bellingham, WA: Elliott Health Care Associates. 2008. Available from: <http://www.elliotthealthcare.com>.

6. Melatonin. *Monograph*. *Altern Med Rev*. 2005;10:326-36.

7. Reiter RJ, Tan DX, Fuentes L. Melatonin: a multitasking molecule. *Prog Brain Res*. 2010;181:127-51.

8. Ohida T, Osaki Y, Doi Y, Tanihata T, Minowa M, Suzuki K, *et al.* An epidemiologic study of self-reported sleep problems among Japanese adolescents. *Sleep*. 2004;27:978-85.

9. Liu X, Uchiyama M, Okawa M, Kurita H. Prevalence and correlates of self-reported sleep problems among Chinese adolescents. *Sleep*. 2000;23:27-34.

10. Seo W, Sung H, Lee J, Koo B, Kim M, Kim S, *et al.* Sleep patterns and their age-related changes in elementary school children. *Sleep Med*. 2010;11:569-75.

11. Short MA, Gradisar M, Lack LC, Wright H, Carskadon M. The discrepancy between actigraphic and sleep diary measures of sleep in adolescents. *Sleep Med*. 2012;13:378-84.

12. Van den J. Television viewing, computer game playing, and Internet use and self-reported time to bed and time out of bed in secondary-school children. *Sleep*. 2004;27:101-4.

13. Schochat T, Flint O, Tzizchinsky O. Sleep patterns, electronic media exposure and daytime sleep-related behaviours among Israeli adolescents. *Acta Paediatr*. 2010;99:1396-400.

14. Van den J. Adolescent use of mobile phones for calling and for sending text messages after lights out: results from a prospective cohort study with a one-year follow up. *Sleep*. 2007;30:1220-3.

15. Praninskiene R, Dumalakiene I, Kemezyz R, Mauricas M, Jucaite A. Diurnal melatonin patterns in children: ready to apply in clinical practice? *Pediatr Neurol*. 2012;46:70-6.

16. Brzezinski A, Vangel MG, Wurtman RJ, Norrie G, Zhdanova I, Ben-Shushan A, *et al.* Effects of exogenous melatonin on sleep: a meta-analysis. *Sleep Med*. 2005;9:41-50.